

Section II (Remarks)

A. Summary of Amendment to the Claims

By the present Amendment, claims 1, 8, and 12 have been amended; and new claims 23 and 24 have been added. Claims 13-22 were withdrawn by the examiner. No new matter within the meaning of 35 U.S.C. §132(a) has been introduced by the foregoing amendments.

The amendments made herein are fully consistent with and supported by the originally-filed disclosure of this application.

B. Response to Rejections Under 35 U.S.C. 112

In the March 8, 2007 Office Action, claim 8 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which application regards as the invention. Specifically, original claim 8 recited the limitation "the temporary sealing step" in claim 1, and there exists insufficient antecedent basis for such limitation in claim 1.

In response to such rejection, claim 8 has been amended to depend from claim 2, which recites "the step of temporarily sealing the fluidic inlet prior to the evacuation step," thus providing antecedent basis for the "temporary sealing step" of claim 8. In view of such amendment, withdrawal of the rejection of claim 8 under 35 U.S.C. 112, second paragraph, is respectfully requested.

C. Response to Rejections Under 35 U.S.C. 102

In the March 8, 2007 Office Action, claims 1, 2, 5, 9, and 10 were rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,875,619 to Blackburn ("Blackburn"). Such rejections are traversed in application to the claims as amended herewith.

1. Law Regarding Anticipation Rejections

"Anticipation requires the disclosure in a single prior art reference of each element of the claim under consideration." *W.L. Gore & Assocs. v. Garlock*, 721 F.2d 1540, 220 USPQ 303, 313 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). It is not enough that the prior art reference

disclose all the claimed elements in isolation. Rather, “anticipation requires the presence in a single prior art reference disclosure of each and every element of the claimed invention, arranged as in the claim.” *Lindemann Maschinenfabrik GmbH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 221 USPQ 481, 485 (Fed. Cir. 1984) (emphasis added). Further, “[u]nder 35 U.S.C. § 102, anticipation requires that ... the prior art reference must be enabling, thus placing the allegedly disclosed matter in the possession of the public.” *Akzo, N.V. v. United States Int’l Trade Comm’n*, 808 F.2d 1471, 1 USPQ2d 1241, 1245 (Fed. Cir. 1986).

3. Patentable Distinctions of Claim 1 Over Blackburn

Blackburn discloses a microfluidic device including a “gas diffusion accelerator” for facilitating diffusion of gas across a flexible gas-permeable barrier. See, e.g., Blackburn col. 72, lines 12-64. A microfluidic device having a gas-permeable barrier 16 bounding a chamber volume 26 containing a sample fluid 26, with the gas-permeable barrier 16 adapted to permit the diffusion of gas from the volume 25, is illustrated in Blackburn Figure 44 as reproduced below.

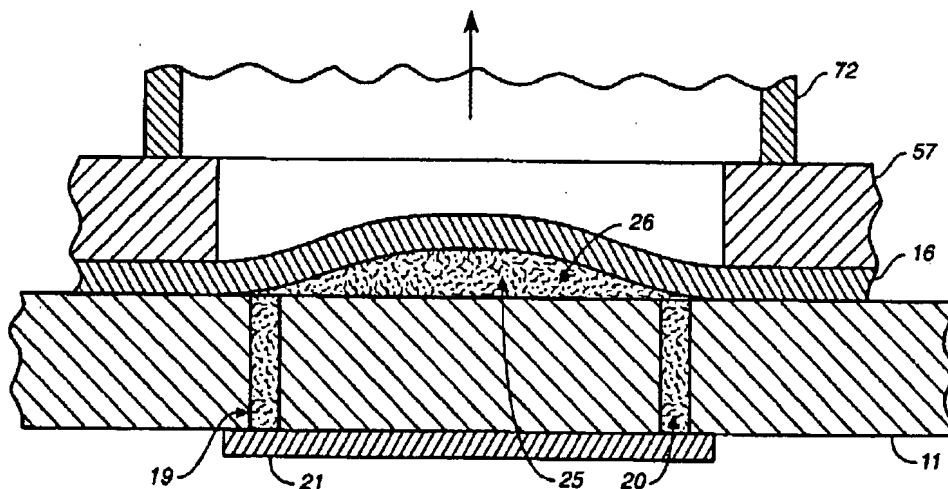


FIG. 44

Blackburn provides that “[t]he gas diffusion accelerator creates a pressure gradient or concentration gradient across [a] flexible, gas permeable layer 16, thereby increasing the rate of diffusion to remove gas bubbles from a gas-containing sample fluid contained in volume 25 across flexible gas-permeable layer [16].” *Id.*, col. 72, lines 47-52. The “flexible gas-permeable membrane layer 16 is selected to have physical, chemical and mechanical properties such that the surface tension at sample fluid 26 prevents passage of the sample fluid through

the pores of the membrane while allowing passage of gas molecules across the flexible, gas permeable layer [16].” In a preferred embodiment “a vacuum source 70 is removably affixed to flexible, gas-permeable layer 16,” with the vacuum source 70 including “a vacuum pump 71, a chamber seal 72 that ... is removably affixed to flexible, gas permeable layer 16, and a length of plastic tubing 73 connecting vacuum pump 71 to reducer 72.” *Id.*, col. 72, lines 56-61.

Thus, Blackburn clearly teaches the removal of gas from a sample (liquid) *already present* in a microfluidic device. This is in sharp contrast to the present invention, which requires removal of gas *prior to* introduction of liquid into a microfluidic device. See amended claim 1 of the instant application, which expressly requires that the liquid introduction step is performed “**following the gas evacuation step.**” Nothing in Blackburn teaches or remotely suggests removal of gas from a microfluidic device prior to introduction of liquid thereto.

The present invention provides numerous advantages over the teachings of Blackburn. Blackburn requires gas diffusion across the a gas-permeable but liquid-impermeable membrane 16. Blackburn’s gas-permeable membrane 16 is not suited for use at elevated operating pressures commonly used in high performance liquid chromatography, as the very properties that make membrane 16 flexible and gas-permeable also render it fragile and subject to rupture at extreme conditions. Moreover, Blackburn’s membrane inherently provides resistance to gas flow, thus extending the time required to evacuate a device as compared to evacuation through an port or channel adapted for liquid flow, as provided in new claims 23 and 24 of the instant application.

Because Blackburn fails to disclose introduction of liquid into a microfluidic device following evacuation of gas from such a device, it fails to teach “each and every element of [claim 1], arranged as in the claim” (*Lindemann, supra*), such that claim 1 cannot be anticipated. Furthermore, because dependent claims inherently include all the limitations of the claims on which they depend, dependent claims 2, 5, 9, and 10 are similarly not anticipated by Blackburn. Accordingly, withdrawal of the rejections of claims 1, 2, 5, 9, and 10 under 35 U.S.C. 102 is warranted, and respectfully requested.

D. Response to Rejections Under 35 U.S.C. 103

The March 8, 2007 Office Action contained multiple rejections under 35 U.S.C. 103, including:

- a rejection of claim 3 as being invalid for obviousness over Blackburn in view of U.S. Patent No. 6,632,619 to Harrison et al. ("Harrison")
- a rejection of claims 4 and 11 as being invalid for obviousness over Blackburn in view of U.S. Patent Application Publication No. 2002/0199094 to Strand et al. ("Strand");
- a rejection of claim 6 as being invalid for obviousness over Blackburn in view of U.S. Patent No. 6,499,499 to Dantsker et al. ("Dantsker"); and
- a rejection of claims 7, 8, and 12 as being invalid for obviousness over Blackburn in view of U.S. Patent No. 6,607,907 to McNeely et al. ("McNeely").

Such rejections are traversed in application to the claims as amended herewith.

1. Law Regarding Obviousness Rejections

To support a rejection under 35 U.S.C. 103, the prior art reference(s) must teach all of the limitations of the claims. MPEP § 2143.03.

In considering a reference for its effect on patentability, the reference is required to be considered in its entirety, including portions of teach away from the invention under consideration. Simply stated, the prior art must be considered as a whole. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984); MPEP § 2141.02. "It is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art." *Application of Wesslau*, 353 F.2d 238, 241 (C.C.P.A. 1965); *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve*, 796 F.2d 443, 448 (Fed. Cir. 1986), *cert. denied*, 484 U.S. 823 (1987).

According to the recent U.S. Supreme Court decision in *KSR International Co. v. Teleflex Inc.*, No. 04-1350, 550 U.S. ____ (April 30, 2007), the court did not disavow the previous "teaching, motivation or suggestion" or "TSM" test, but stated that such TSM test *should not be strictly applied* in determining obviousness. In connection with this point, the Supreme Court stated that:

"A patent composed of several elements is not proved obvious merely by demonstrating that each element was, independently, known in the prior art. ... [Rather], it can be important to identify a reason that would have

prompted a person of ordinary skill in the relevant art to combine the [prior art] elements in the manner claimed." *KSR*, slip op. at 14.

It is fundamental to a proper rejection of claims under 35 U.S.C. 103 that an examiner must present a convincing line of reasoning ~~supporting the rejection.~~ MPEP 2144 ("Sources of Rationale Supporting a Rejection Under 35 U.S.C. 103"), citing *Ex parte Clapp*, 227 USPQ 972 (Bd. Pat. App. & Inter. 1985). The Supreme Court in *KSR* affirmed the validity of such approach, stating that "there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness."

In *KSR*, the Supreme Court further confirmed that references that teach away from the invention are evidence of the non-obviousness of a claimed invention, (*KSR*, slip op. at pp. 20-23) and reaffirmed the principle that a factfinder judging patentability "should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning."

2. Claim 3 is Not Obvious Over Blackburn and Harrison

Harrison has been cited by the examiner as disclosing a microfluidic device containing air. March 8, 2007 Office Action, page 3. Harrison discloses the addition of phosphate buffered saline to microfluidic flow paths, and flushing such solution through the microfluidic device with continuous vacuum to remove air bubbles from the flow paths. Harrison, col. 19, lines 46-51. Thus, Harrison clearly teaches the removal of gas from a liquid *already present* in a microfluidic device, rather than removal of gas *prior to* introduction of liquid into a microfluidic device as required by claim 3. Nothing in Harrison teaches or remotely suggests removal of gas from a microfluidic device prior to introduction of liquid thereto. Because Harrison fails to remedy Blackburn's failure to teach introduction of liquid into a microfluidic device following evacuation of gas from such a device, no combination of Blackburn and Harrison teach all of the limitations of claim 3, as would be required by MPEP § 2143.03 to support a *prima facie* case of obviousness. Accordingly, withdrawal of the rejection of claim 3 under 35 U.S.C. 103 is warranted, and respectfully requested.

3. Claims 4 and 11 are Not Obvious Over Blackburn and Strand

Strand has been cited by the examiner as disclosing a method of separating fluids in a cartridge using separation media comprising stationary phase material that allows for reversible adsorption of species in the fluid. March 8, 2007 Office Action, page 4; Strand, paragraph 10. Nothing in Strand teaches or remotely suggests removal of gas from a microfluidic device prior to introduction of liquid thereto. Because Strand fails to remedy Blackburn's failure to teach introduction of liquid into a microfluidic device following evacuation of gas from such a device, no combination of Strand and Harrison teach all of the limitations of claims 4 and 11, as would be required by MPEP § 2143.03 to support a *prima facie* case of obviousness. Accordingly, withdrawal of the rejections of claims 4 and 11 under 35 U.S.C. 103 is warranted, and respectfully requested.

4. Claim 6 is Not Obvious Over Blackburn and Dantsker

Dantsker has been cited by the examiner as disclosing a method for flow control in multistream microfluidic devices having a plurality of inlets, a plurality of microphonic channels, and a plurality of outlets, and the introduction into a microfluidic device of insolvent comprising ethanol. March 8, 2007 Office Action, page 5. Nothing in Dantsker teaches or remotely suggests removal of gas from a microfluidic device prior to introduction of liquid thereto. Because Dantsker fails to remedy Blackburn's failure to teach introduction of liquid into a microfluidic device following evacuation of gas from such a device, no combination of Blackburn and Dantsker teach all of the limitations of claims 4 and 11, as would be required by MPEP § 2143.03 to support a *prima facie* case of obviousness. Accordingly, withdrawal of the rejections of claims 4 and 11 under 35 U.S.C. 103 is warranted, and respectfully requested.

5. Claims 7, 8, and 12 are Not Obvious Over Blackburn and McNeely

McNeely has been cited by the examiner as disclosing the step of disallowing fluid communication between a vacuum source and at least one of a fluidic inlet and a fluidic outlet prior to introduction of liquid into a microfluidic device. March 8, 2007 Office Action, page 6.

In one embodiment, McNeely discloses the use of a downstream valve that acts as a selectively operable air vent that may be closed to permit pressure to be elevated within the device. :

Fluid circuit 40 is filled with water up to a series of parallel processing chambers 10 and 11. Air displacement ducts 30 and 31 are joined into a single air

displacement duct 32 and connected to the system outlet 33. A valve 36 connected to the outlet tubing 37 is opened to allow for air to be displaced out of the system as it fills with liquid fluid. Once chambers 10 and 11 are filled, the system is pressurized by pumping air via a pressure regulation device 34 (which may be, for example, a syringe) connected to outlet tubing 37 into circuit 40 via the outlet 33. A pressure gauge 35 may be connected to the system to indicate the pressure reached, and to monitor pressure during cycling. Once the desired pressure is reached, valve 36 may be closed and pressure regulation device 34 removed or turned off.

McNeely, col. 5, lines 53-66.

In another embodiment, McNeely discloses the use of a slight air flow passed in and out of a microfluidic circuit by a cross channel, to remove steam or other vapor generated by a heating process. Such embodiment is described in connection with McNeely Fig. 6, as reproduced below.

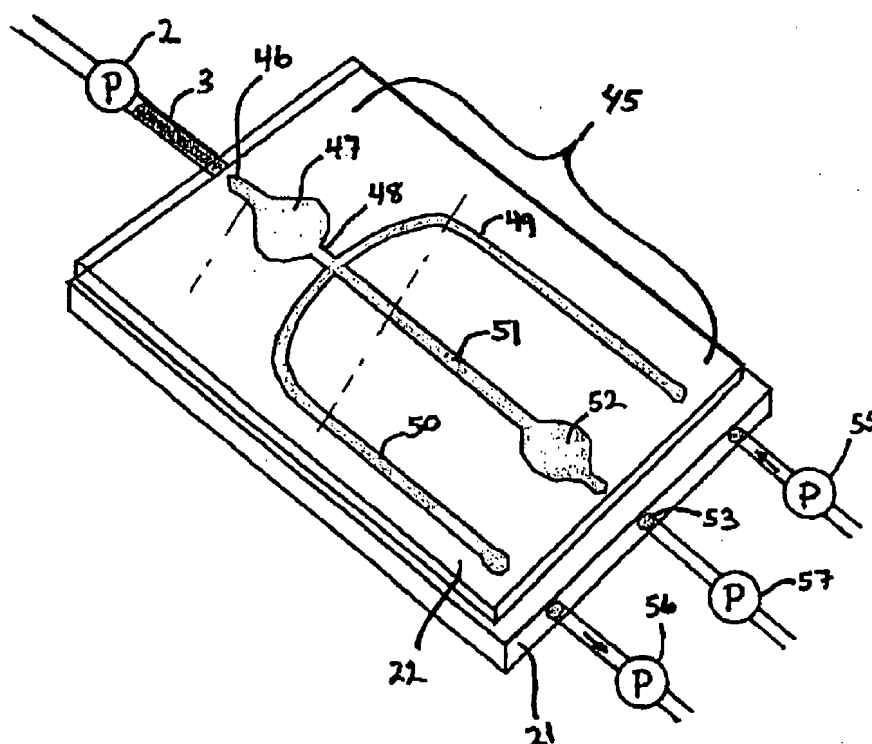


FIG. 6

“FIG. 6 illustrates an alternative embodiment of the invention which makes it possible to remove steam (or other vapor) generated by a heating process by a slight air flow caused by air being passed in and out of the microfluidic circuit by a cross channel. FIG. 6 shows microfluidic circuit 45 with one inlet 46

leading to reaction chamber 47 with one outlet 48. Near outlet 48 are two cross channels 49 and 50, which function as air ducts. **Air flows into the system via first air duct 49, driven by positive pressure from pressure regulation device 55. The air from air duct 49 crosses main microchannel 51 between reaction chambers 47 and 52 in the vicinity of reaction chamber 47, and is drawn out of the system via second air duct 50, due to negative pressure from pressure regulation device 56.**"

McNeely, col. 6, lines 6-19.

McNeely states that a vapor within the microfluidic device is "generated by a heating process." This inherently requires the initial presence of liquid in the device to generate such a vapor. It is only *after* such liquid is present that McNeely circulates air through cross channels 49 and 50 to withdraw vapor from the device. Moreover, McNeely describes passage or pumping of air in and out of the device at the same rate (e.g., McNeely, col. 6, lines 30-31) to accelerate evaporation. Because air is pumped into the device as it is withdrawn, McNeely fails to achieve any evacuated condition within a microfluidic device in such embodiment.

In yet another embodiment, McNeely describes the addition of a "solvent mixture [to] a microfluidic evaporation chamber connected to one or more air ducts," with the air duct being "connected to a vacuum pump and the internal pressure is slowly lowered to allow for accelerated and controlled evaporation on a micro scale." McNeely, col. 6, lines 40-45. Such embodiment teaches that **liquid is added to a microfluidic device *first***, and thereafter vacuum is applied to accelerate evaporation.

Accordingly, nothing in McNeely teaches or remotely suggests removal of gas from a microfluidic device prior to introduction of liquid thereto. Because McNeely fails to remedy Blackburn's failure to teach introduction of liquid into a microfluidic device following evacuation of gas from such a device, no combination of Blackburn and McNeely teach all of the limitations of claims 7, 8, and 12, as would be required by MPEP § 2143.03 to support a *prima facie* case of obviousness. Accordingly, withdrawal of the rejections of claims 7, 8, and 12 under 35 U.S.C. 103 is warranted, and respectfully requested.

E. Fee Payable for Added Claims

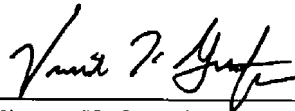
By the present Amendment, no new independent claims and two new total claims have been introduced, beyond the numbers for which payment was previously made. Small entity fees payable for such added claims are calculated as follows: $2 \times \$25.00 = \50.00 .

Payment of such excess claim fees is authorized in the enclosed Credit Card Payment Form PTO-2038.

CONCLUSION

Based on the foregoing, all of Applicants' pending claims 1-12 and 23-24 are patentably distinguished over the art, and in form and condition for allowance. The examiner is requested to favorably consider the foregoing, and to responsively issue a Notice of Allowance. If any issues require further resolution, the examiner is requested to contact the undersigned attorney at (919) 419-9350 to discuss same.

Respectfully submitted,



Vincent K. Gustafson
Reg. No. 46,182
Attorney for Applicants

INTELLECTUAL PROPERTY/
TECHNOLOGY LAW
Phone: (919) 419-9350
Fax: (919) 419-9354
Attorney File No.: 4270-129

Enclosures:

Credit Card Form PTO-2038 authorizing \$110.00[1 pg.]

<p>The USPTO is hereby authorized to charge any deficiency or credit any overpayment of fees properly payable for this document to Deposit Account No. 08-3284</p>
--